

# Cytokine storm treated successfully with immunoglobulin therapy in a pregnant COVID-19 patient

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**ABSTRACT**

Ever since its emergence Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV 2) has caused an enormous amount of morbidity and mortality. Pregnancy being a high risk state is also being affected by this lethal pandemic causing an increased risk of rising maternal mortality. The treatment strategies for managing COVID-19 in pregnant female remains limited with no definite treatment available. With the growing evidence of Lymphocytopenia in COVID-19 there has been a emergence of immunoglobulin (IVIg) as a relatively safe treatment option in immunodeficient states such as pregnancy. Though research remains limited in the aspect of immunoglobulin therapy in pregnancy a risk versus benefit ratio might allow use of immunoglobulin therapy. We present a case of COVID-19 associated cytokine storm with lymphocytopenia in a Pregnant female which was successfully treated with Immunoglobulin therapy.

**Keywords:** COVID-19, pregnancy, immunoglobulin therapy

**1. INTRODUCTION**

With the continuously growing wrath of COVID-19 pandemic there has been a lookout for treatment options to reduce mortality and morbidity. Although, it has been more than a year since its spread Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) is proving to be a challenge for health care professionals throughout the world. Treatment modalities like antiviral medications, monoclonal antibodies and intravenous immunoglobulin are being given trial throughout the world. However, there is no proved therapy for COVID-19 yet and symptomatic treatment remains the line of management for patients. One of the common laboratories finding in COVID-19 patients remains to be lymphocytopenia. Patients who have lymphocytopenia are on increased risk of having more severe infection and lack of immunity may also give rise to secondary infections like bacterial or fungal infections. Immunoglobulins are highly diverse molecules which provide immunity in various conditions including physiological as well as pathological etiologies. Immunoglobulins play a vital role in maturation of B

and T lymphocytes which form the main defense mechanism of the body (Yockey and iwasaki 2018).

Polyclonal immunoglobulins are being used a treatment in various different diseases with primary and secondary hypogammaglobulinemia, recurrent infections, malignancy and neuropathies. Also, polyclonal immunoglobulins were reported to activate various subpopulations of T cells with great impact on proliferation of T cells, its survival and its function during lymphocytopenia. IVIg has also been used against virus bacteria as well as fungi. In the current scenario they are being given as a therapy for COVID-19. In the cytokine storm, IVIg could bring down the inflammation by improving function of lymphocytes. Although the results are not well established but the increasing evidence of cytokine storm associated mortality with lymphocytopenia could warrant the use of IVIg after a full risk benefit ratio assessment by the treating physician. Pregnancy, although not an immunodeficient state in classical sense, immunological changes in pregnancy might lead to a state of increased susceptibility to intracellular pathogens such as Virus (Chen et al., 2020). Immune response of the placenta as well as its tropism for certain pathogens and virus may complicate the disease course of COVID-19.

Hence, treating a Cytokine Storm with IVIg In a pregnant female remains a complex decision to be made by the physicians and requires a thorough approach with full assessment of the pros and cons. We report a case of a pregnant female who presented with severe COVID-19 with hypoxia and was successfully treated with IVIg.

## 2. CASE REPORT

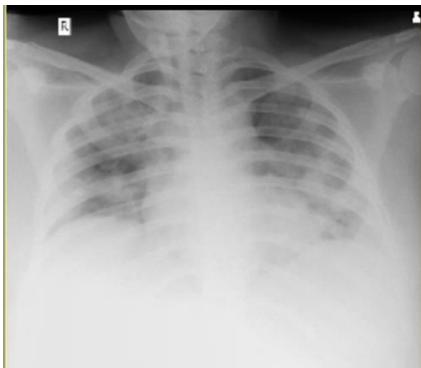
A 25 year old Primi Gravida with 28 Weeks of gestational age presented with the chief complaint of fever with breathlessness since four days. There was no history of Hypertension, Diabetes Mellitus or thyroid disorder in the past. Obstetric History revealed duration of marriage to be one year. Obstetric history revealed duration of marriage 1 year, primi, two tetanus injections received. Menstrual history revealed last menstrual period 30 weeks prior to her admission. On examination the patient was afebrile, respiratory rate was 28 breaths per minute, pulse was 112/min, regular in rhythm, blood pressure was 120/84 mm hg in right arm supine position and spo<sub>2</sub> was 80 percent on room air. On systemic examination uterus was 28 weeks in size, relaxed, cephalic, Fetal heart sound were present, 148 beats per minute, Heart sounds were normal, Patient was conscious and oriented and chest was bilateral clear. Laboratory Investigations were indicative of increased inflammatory markers (table 1).

Chest X ray showed extensive bilateral infiltration (figure 1). A nasopharyngeal swab was sent for testing of COVID-19 by RTPCR method which turned out to be positive. Patient was taken on non-invasive ventilation in view of falling saturation. Patient was started on Antibiotics, Low molecular Weight Heparin and other supportive treatment and was also given intravenous immunoglobulin after assessment of risk benefit ratio. Oxygen was titrated and patient was taken off non invasive ventilation, patient was then shifted to high flow oxygen which was tapered and ultimately stopped. Throughout the hospital stay, Fetal Heart Sounds were present and were normal. Patient was discharged after 20 days of hospital admission with a Chest X Ray showing clearing (figure 2).

**Table 1** Showing Lab Investigations of the Case

CBC	Hb-11.7gm/dl MCV-84fl Platelet count-96000/dl WBC Count- 3300/dl(lymphocytes 400/dl)
LFT	Total Protein-6.2gm/dl, Albumin3.2gm/dl, Globulin3.2gm/dl, aspartate aminotransferase 23 units/l, alanine aminotransferase 21 units/l, Alkaline Phosphatase99 IU/l, Total Bilirubin :1.1mg/

KFT	Creatinine:0.7mg/dl, Urea36mg/dl, Sodium133mmol/l, Potassium -4.1mmol/l
CRP	66.0mg/dl
D-Dimer	1.11
Serum Ferritin	770ng/ml



**Figure 1** Showing Chest X ray with bilateral infiltration on admission



**Figure 2** Showing Chest X ray with clearing post IVIg therapy after 20 days of admission

### 3. DISCUSSION

Immunity during pregnancy is a complex aspect with placental immune response and its tropism for various virus and pathogens. It is interesting to note that Angiotensin Convertase Enzyme 2 receptors have been found on the placenta. This receptor is used by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV 2) for modulating its effect (Heymann et al., 2020). Presence of the receptor which is used to manifestation of pathogenic effects by the SARS CoV 2 on Placenta might justify the severe COVID-19 infection encountered in our patient. Increased risk for thrombosis and microangiopathy in COVID-19 might further complicate the pregnancy (Jain et al., 2020). There was severe hypoxia with bilateral infiltration which led to a decision of using Intravenous Immunoglobulin in our patient. There was drastic improvement in our case following IVIg therapy, indicating the benefit of IVIg therapy. IVIg is a product of the blood which is prepared from the COVID-19 recovered patient's serum. The major component of this Intravenous immunoglobulin is IgG antibody which has subclass of IgG1 and IgG2. However, scanty amount of other immunoglobulins like IgA and IgM can also be found. The actual physiology behind the function of immunoglobulin is by the boost it provides to the immunity thus it leads to a decrease in the profound inflammatory action seen in COVID-19. This Cytokine Storm is the main pathophysiology behind the acute lung injury witnessed in COVID-19 (Talwar, 2021). The research behind its efficacy and safety in Pregnancy is limited however in a case of severe COVID-19 with cytokine storm an assessment was made with proper laying out of pros and cons and it was given in pregnancy.

There was drastic improvement in the patient following intravenous immunoglobulin thus indicating its efficacy. Given the rationale of cytokine storm and its role in increasing mortality in COVID-19 we highlight the benefits and need to add Immunoglobulins in the treatment protocol for COVID-19.

### 4. CONCLUSION

We conclude that even though there is limited research in terms on IVIg usage in Pregnancy its use is justified in a case of acute respiratory distress caused by COVID-19 to save the life of patient. Fortunately no harmful effects were witnessed on the fetus in our case and the patient recovered completely and was discharged in stable condition. Hence the treating physicians should definitely consider Immunoglobulin therapy in treatment of Severe COVID-19.

#### Acknowledgement

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#### Conflict of interest

The Authors have no conflicts of interest that are directly relevant to the content of this clinic-pathological case

#### Financial Resources

There are no financial resources to fund this study

#### Informed Consent

Informed Consent was obtained from the patient.

#### Author's contribution

All the authors contributed equally to the case report.

#### Data and materials availability

All data associated with this study are present in the paper.

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